UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,253	01/26/2005	Samual Weiss	16601-021US1	8661

26181 7590 12/28/2006
FISH & RICHARDSON P.C.
PO BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
MCGILLEM, LAURA L	
ART UNIT	PAPER NUMBER
1636	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/28/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,253	WEISS, SAMUAL	
	Examiner	Art Unit	
	Laura McGillem	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *19-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/21/05, 1/26/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date: _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I (claims 1-18) in the reply filed on 11/21/2006 is acknowledged.

Claims 19-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/21/2006.

Claims 1-18 are under examination.

Priority

It is noted that this application is the national phase application of International Application No. PCT/CA2003/001151, filed July 30, 2003, which receives priority benefit of U.S. Provisional Application No. 60/399,192, filed July 30, 2002.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 6, 9, 12, 14-15 and 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Mehler et al (of record).

Mehler et al teach a method to differentiate oligodendrocytes, neurons and astrocytes from a neural stem and progenitor cell line (see page 214, 2nd paragraph, for example). Mehler et al teach that application of cytokines such as G-CSF significantly increase survival and promotes differentiation from neural stem cells into oligodendrocytes (see page 230, 4th paragraph, for example) which anticipates a method of producing oligodendrocytes from mammalian multipotent neural stem cells comprising contacting the cells with an effective amount of at least one oligodendrocyte promoting factor such as G-CSF, and meets the limitations of claims 1-2.

Mehler et al teach the method using a neural stem and progenitor cell line obtained from murine embryonic brain regions including hippocampus, striatum, cortex and hypothalamus (see pages 219, 4th paragraph and page 220, 1st and 3rd paragraph, for example) which meets the limitation of using a cell culture of multipotent neural stem cells prepared from mammalian (rodent) brain tissue specifically from the subventricular zone, defined in the instant specification as the subventricular zone of the forebrain and anticipates claims 6, 9 and 12.

Mehler et al teach that cells can be induced to differentiate to oligodendrocytes in cultures containing bFGF, PDGFAA, and IGF-1 for example (see page 214, table 1). Mehler et al teach embodiments of the differentiation method comprising addition of growth factors such as bFGF, IGF1 or CTNF to the cell culture either in a pretreatment or simultaneously in order to increase the frequency and maturation of oligodendrocytes

(see page 230, 4th paragraph and page 231, for example), which meets the limitations of a method comprising the step of adding at least one biological agent capable of increasing the number of neural stem cells wherein the agent is selected from the group of FGF1, bFGF or CNTF, and wherein the cells are contacted concurrently or wherein prior to the contact with G-CSF and anticipates claims 14-15 and 17-18. Absent evidence to the contrary, FGF1, bFGF or CNTF would be capable of increasing the number of neural stem cells.

Claims 1-2, 5, 12-15 and 17-18 are rejected under 35 U.S.C. 102(e) as being anticipated by Tennekoon et al (U.S. Patent No. 6,673,606, filed 4/12/2001, of record).

Tennekoon et al teach that mesenchymal stromal cells (MSC) can differentiate into oligodendrocytes (see column 2, lines 35-40, for example). Tennekoon et al teach that MSC cells have stem cell like qualities such as pluripotency. Tennekoon et al teach a method to differentiate human and rat MSC into oligodendrocytes and neurons under appropriate culture conditions by adding or removing various trophic factors to effect oligodendrocytal differentiation (see column 3, lines 5-25 and column 15, Example 1 and column 16, Example 4, in particular). Absence evidence to the contrary, a cell that can differentiate into oligodendrocytes and neurons is inherently a multipotent neural stem cell. Tennekoon et al teach that MSC are isolated from bone marrow and cultured in medium suited for oligodendrocyte differentiation and proliferation. Tennekoon et al teach that cytokines and growth factors are especially relevant to differentiating MSC into oligodendrocytes including colony stimulating factors such as G-CSF (see column

6, lines 52-67 and, column 7, lines 30-45, for example) which meet the limitations of a method of producing oligodendrocytes from mammalian multipotent neural stem cells comprising contacting cultured neural stem cells with an effective amount of oligodendrocyte promoting factor wherein the OPF is G-CSF and the cells are human or rat cells and therefore anticipates claims 1-2, 5, and 12-13.

Tennekoon et al teach that CNTF can be added to the culture (see column 6, lines 63-67, for example). Tennekoon et al also teach that the MSC culture medium can comprising tri-iodothyronine (see column 6, lines 40-45) which meets the limitation of claim 4. Tennekoon et al teach that bFGF, FGF2, EGF, TGF-α and IGF-1 will promote cellular proliferation (see column 4, lines 2-11, column 6, lines 52-67 and column 7, lines 1-5 for example) which meets the limitations of the claimed method further comprising contacting the cells with at least one biological agent (e.g. EGF, FGF, TGF1, CTNF and IGF-1) capable of increasing the number of stem cells and anticipates claims 14-15.

Absent evidence to the contrary, the biological factors and oligodendrocyte promoting factors are present in the culture medium and therefore contact the neural stem cells concurrently and anticipate claim 17. Also, Tennekoon et al teach an embodiment in which the undifferentiated cells are pretreated with growth factors before subsequent addition of cytokines (see column 7, lines 22-30, for example) which meets the limitations of the claimed method wherein the neural stem cells are contacted with a biological agent prior to the oligodendrocyte promoting factor and anticipates claim 18.

Claims 1-3 and 5-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Bjornson et al (U.S. Patent No. 6,897,060, filed 7/24/2000).

Bjornson et al teach multipotent neural stem cells (MNSC) that can be induced to differentiate into oligodendrocytes, astrocytes and neurons in an appropriate environment to influence the growth and development if MNSC and their progeny (see column 4, lines 13-44, for example). Bjornson et al teach an embodiment of a differentiation method in which an MNSC culture or composition conditions can comprise hematopoietic growth factors such as GM-CSF or G-CSF to accelerate the period in which certain cell types are generated (see column 8, lines 55-65, for example), which reads on a method of producing oligodendrocytes from a mammalian multipotent neural stem cells by contacting the cultured MNSC with an oligodendrocyte promoting factors such as GM-CSF or G-CSF to produce oligodendrocytes and therefore anticipates claims 1-3.

Bjornson et al teach that precursor cells can be derived from embryonic, post-natal, juvenile or adult mammalian tissue, including neural tissue from the cerebral cortex, frontal lobe, hypothalamus and tissues surrounding ventricles of the central nervous system (see column 2, lines 55-67, for example) which reads on MNSC provided as a cell culture prepared using mammalian brain tissue from a non-embryonic mammal or an adult mammal, especially from the subventricular zone and anticipates claims 5-9. Bjornson et al further teach that the environment for MNSC differentiation can be performed *ex vivo* or *in vivo* (see column 4, lines 45-55, for example), which reads on the claimed method of differentiation wherein the MNSC are located in a

mammal, such as the subventricular zone of a mammal and anticipates claims 10-11. Bjornson et al teach an embodiment of the method in which MNSC cells are obtained from embryonic and adult mice as well as human biopsies (see column 9, example 1, and column 17, example 7, for example), which meets the limitation of the claimed method wherein the MNSC are from humans and rodents and anticipates claim 12.

Bjornson et al teach that the MNSC cells can be induced to proliferate by culturing in medium that contains EGF and FGF (see column 5, lines 55-65, for example) which reads on the claimed method of differentiating MNSC cell to oligodendrocytes by contacting the cells with a biological agent such as EGF or FGF capable of increasing the number of MNSC and anticipates claims 13-15.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tennekoon et al (of record) in view of Magil et al (U.S. Patent Application No. 20030171269, filed 10/23/2001).

The teachings of Tennekoon et al are discussed in the above rejection Tennekoon do not teach the use of EGF51N as a biological agent.

Magil et al teach that full length wild-type human EGF is a 53 amino acid protein that is susceptible to proteases (see paragraph 0002, for example). Magil et al teach a polypeptide having 51 residues, known as EGF51N, with the biological activity of EGF and has an amino acid at the carboxyl terminus that is capable of conferring resistance to proteolysis (see paragraphs 0018 and 0046, for example). Magil et al teach that modification of the C-terminus of EGF protects EGF from proteolysis and maintains at least two biological activities (see paragraph 066, for example).

It would have been obvious to the skilled artisan at the time the invention was made to use EGF51N as taught by Magil et al as a biological agent in a method to produce oligodendrocytes from stem cells as taught by Tennekoon et al because Magil et al teach that wild type EGF is susceptible to cleavage by native proteases and EGF51N is protease resistant. The motivation to use EGF51N as a biological agent is the expected benefit of being able to increase the number of multipotent neural stem cells in culture with a modified amino acid sequence of EGF that is more resistant to proteolysis than a natural identical EGF and retains the biological activity of EGF. There is a reasonable expectation of success to use EGF51N in a method to produce oligodendrocytes since it has worked previously in the cited references. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura McGillem whose telephone number is (571) 272-8783. The examiner can normally be reached on M-F 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Laura McGillem, PhD
12/22/2006

DANIEL M. SULLIVAN
PATENT EXAMINER